

AMENDMENT TO THE CLAIMS

1. (Withdrawn) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

- (a) a polynucleotide encoding amino acids from about 1 to about 251 of SEQ ID NO:4;
- (b) a polynucleotide encoding amino acids from about 2 to about 251 of SEQ ID NO:4;
- (c) a polynucleotide encoding amino acids from about 1 to about 24 of SEQ ID NO:4;
- (d) a polynucleotide encoding amino acids from about 25 to about 251 of SEQ ID NO:4;
- (e) a polynucleotide encoding amino acids from about 1 to about 175 of SEQ ID NO:4;
- (f) a polynucleotide encoding amino acids from about 1 to about 178 of SEQ ID NO:4;
- (g) a polynucleotide encoding amino acids from about 177 to about 251 of SEQ ID NO:4;
- (h) a polynucleotide encoding amino acids from about 180 to about 251 of SEQ ID NO:4;
- (i) the polynucleotide complement of (a), (b), (c), (d), (e), (f), (g) or (h); and
- (j) a polynucleotide at least 90% identical to the polynucleotide of (a), (b), (c), (d), (e), (f), (g) or (h).

2. (Withdrawn) An isolated nucleic acid molecule which comprises 20-753 contiguous nucleotides from the coding region of SEQ ID NO:3.

3. (Withdrawn) The isolated nucleic acid molecule of claim 2, which comprises 60-500 contiguous nucleotides from the coding region of SEQ ID NO:3

4. (Withdrawn) The isolated nucleic acid molecule of claim 3, which comprises 200-300 contiguous nucleotides from the coding region of SEQ ID NO:3.

5. (Withdrawn) An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has an amino acid sequence selected from the group consisting of:

- (a) amino acids from about 1 to about 251 of SEQ ID NO:4;
- (b) amino acids from about 2 to about 251 of SEQ ID NO:4;
- (c) amino acids from about 1 to about 24 of SEQ ID NO:4;
- (d) amino acids from about 25 to about 251 of SEQ ID NO:4;
- (e) amino acids from about 1 to about 175 of SEQ ID NO:4;
- (f) amino acids from about 1 to about 177 of SEQ ID NO:4;
- (g) amino acids from about 177 to about 251 of SEQ ID NO:4; and
- (h) amino acids from about 180 to about 251 of SEQ ID NO:4.

6. (Withdrawn) The isolated nucleic acid molecule of claim 1, which is DNA.

7. (Withdrawn) A method of making a recombinant vector comprising inserting a nucleic acid molecule of claim 1 into a vector in operable linkage to a promoter.

8. (Withdrawn) A recombinant vector produced by the method of claim 7.

9. (Withdrawn) A method of making a recombinant host cell comprising introducing the recombinant vector of claim 8 into a host cell.

10. (Withdrawn) A recombinant host cell produced by the method of claim 9.

11. (Withdrawn) A recombinant method of producing a polypeptide, comprising culturing the recombinant host cell of claim 10 under conditions such that said polypeptide is expressed and recovering said polypeptide.

12. (Currently Amended) An isolated polypeptide, the amino acid sequence of which comprises a sequence at least 95% identical to amino acids from 1 to 251 of SEQ IS NO:4, wherein said polypeptide retains the a biological activity of human FGF-23, wherein said biological activity is defined as the ability of said isolated polypeptide to lower serum phosphate levels in a mouse administered with said isolated polypeptide, and wherein said administered polypeptide is non-cleavable between amino acid positions 176 and 179 during expression.

13. (Currently Amended) An isolated polypeptide having 251 amino acids, wherein the amino acid sequence of said polypeptide ~~which comprises amino acids from 1 to 251~~ of differs from SEQ ID NO:4; wherein ~~at least one amino acid differs~~ by conservative

substitution of one amino acid from the corresponding position in SEQ ID NO:4, ~~wherein said polypeptide retains the biological activity of human FGF-23.~~

14. (Previously Amended) An isolated and purified polypeptide, the amino acid sequence of which comprises amino acids from 1 to 251 of SEQ ID NO:4.

15. (Currently Amended) ~~An amino acid sequence comprising epitope-bearing portion of the polypeptide of SEQ ID NO:4, wherein said epitope bearing portion~~ An isolated and purified polypeptide comprisinges at least 14 contiguous amino acids of SEQ ID NO:4.

16. (Currently Amended) ~~The amino acid sequence of claim 15, wherein said epitope bearing portion comprises~~ An isolated and purified polypeptide comprising between 10 and 50 contiguous amino acids of SEQ ID NO:4.

17. (Currently Amended) ~~The amino acid sequence of~~ The polypeptide of claim 15, ~~wherein the epitope bearing portion comprising~~es amino acids RRHTRSAEDDSERD (SEQ ID NO:19).

18. (Currently Amended) ~~The amino acid sequence~~ polypeptide of claim 15, ~~wherein the epitope bearing portion comprising~~es the epitope bearing portion comprises amino acids YHLQIHKNGHVDGAPHQ (SEQ ID NO:20).

19. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 12.

20. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 13.

21. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 14.

22. (Original) A pharmaceutical composition comprising the polypeptide of claim 12, in combination with a pharmaceutically acceptable carrier.

23. (Withdrawn) A method for providing trophic support for cells in a patient in need thereof, the method comprising administering to the patient a composition comprising a polynucleotide encoding the polypeptide of SEQ ID NO:4.

24. (Withdrawn) The method of claim 23 wherein said polynucleotide is administered by implanting cells which express said polynucleotide into the patient, wherein said cells express FGF-23 polypeptide in the patient.

25. (Withdrawn) The method of claim 23 wherein the implanted cells are encapsulated in a semipermeable membrane.
26. (Withdrawn) The method of claim 23 wherein the patient suffers from a condition characterized by dysfunction of or injury to skin cells.
27. (Withdrawn) The method of claim 23 wherein the condition is traumatic injury.
28. (Withdrawn) The method of claim 23 wherein said patient suffers from a condition characterized by inadequate function of placental cells.
29. (Withdrawn) The method of claim 28 wherein said condition is at least one condition selected from the group consisting of congenital defects, fertility, or abnormal growth.
30. (Withdrawn) The method of claim 23 wherein the patient suffers from a condition characterized by inadequate function of the thymus.
31. (Withdrawn) The method of claim 30 wherein said condition is at least one condition selected from the group consisting of leukemia, lymphoma, autoimmune disease, proliferative disorder of the thymus, and differentiation disorder of the thymus.
32. (Withdrawn) A method for providing trophic support for cells in a patient in need thereof, the method comprising administering to the patient a composition comprising a polypeptide of SEQ ID NO:4.
33. (Withdrawn) The method of claim 28 wherein the patient suffers from a condition characterized by central nervous system disorder.
34. (Withdrawn) The method of claim 29 wherein the condition is selected from the group consisting of Parkinson's disease and Alzheimer's disease.
35. (Withdrawn) A method of alleviating a disease condition in the brain of a human patient wherein said disease condition is alleviated by at least one method selected from the group consisting of slowing degeneration of, restoring function of, and increasing the number of, functional neuronal cells in said human patient, said method comprising administering to said patient a pharmaceutically effective composition comprising a polypeptide having the amino acid sequence of SEQ ID NO:4.
36. (Withdrawn) A method of alleviating a disease condition in the thymus of a human patient wherein said disease condition is alleviated by at least one method selected from

the group consisting of preventing degeneration of, slowing degeneration of, increasing the number of, functional thymic cells in said human patient, said method comprising administering to said patient a pharmaceutically effective composition comprising a polypeptide having the amino acid sequence of SEQ ID NO:4.

37. (Withdrawn) A method of alleviating a disease condition in the skin of a human patient wherein said disease condition is alleviated by at least one method selected from the group consisting of preventing degeneration of, slowing degeneration of, and increasing the number of, functional skin cells in said human patient, said method comprising administering to said patient a pharmaceutically effective composition comprising a polypeptide having the amino acid sequence of SEQ ID NO:4.

38. (Withdrawn) A method of alleviating a disease condition in the placenta of a human patient wherein said disease condition is alleviated by at least one method selected from the group consisting of preventing degeneration of, slowing degeneration of, and increasing the number of, functional placental cells, said method comprising administering to said patient a pharmaceutically effective composition comprising a polypeptide having the amino acid sequence of SEQ ID NO:4.

39. (Withdrawn) A kit for detecting the presence of mRNA encoding FGF-23 in a sample from a patient, said kit comprising a polynucleotide having at least 20 contiguous nucleotides of the polynucleotide of claim 3, packaged in a container.

40. (Withdrawn) The kit according to claim 39 wherein the polynucleotide encodes at least six contiguous amino acids of SEQ ID NO:4.

41. (Withdrawn) A kit for detecting the presence of FGF-23 polypeptide in a sample from a patient, said kit comprising an antibody according to claim 19, packaged in a container.

42. (Withdrawn) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

- (a) a polynucleotide encoding amino acids from about 1 to about 251 of SEQ ID NO:2;
- (b) a polynucleotide encoding amino acids from about 2 to about 251 of SEQ ID NO:2;
- (c) a polynucleotide encoding amino acids from about 1 to about 24 of SEQ

ID NO:2;

- (d) a polynucleotide encoding amino acids from about 25 to about 251 of SEQ

ID NO:2;

- (e) a polynucleotide encoding amino acids from about 1 to about 175 of SEQ

ID NO:2;

- (f) a polynucleotide encoding amino acids from about 1 to about 178 of SEQ

ID NO:2;

- (g) a polynucleotide encoding amino acids from about 177 to about 251 of

SEQ ID NO:2;

- (h) a polynucleotide encoding amino acids from about 180 to about 251 of

SEQ ID NO:2;

- (i) the polynucleotide complement of (a), (b), (c), (d), (e), (f), (g) or (h); and

- (j) a polynucleotide at least 90% identical to the polynucleotide of (a), (b),

(c), (d), (e), (f), (g) or (h).

43. (Withdrawn) An isolated nucleic acid molecule which comprises 20-753 contiguous nucleotides from the coding region of SEQ ID NO:1.

44. (Withdrawn) The isolated nucleic acid molecule of claim 43, which comprises 60-500 contiguous nucleotides from the coding region of SEQ ID NO:1.

45. (Withdrawn) The isolated nucleic acid molecule of claim 44, which comprises 200-300 contiguous nucleotides from the coding region of SEQ ID NO:1.

46. (Withdrawn) An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has an amino acid sequence selected from the group consisting of:

- (a) amino acids from about 1 to about 251 of SEQ ID NO:2;
- (b) amino acids from about 2 to about 251 of SEQ ID NO:2;
- (c) amino acids from about 1 to about 24 of SEQ ID NO:2;
- (d) amino acids from about 25 to about 251 of SEQ ID NO:2;
- (e) amino acids from about 1 to about 175 of SEQ ID NO:2;
- (f) amino acids from about 1 to about 177 of SEQ ID NO:2;
- (g) amino acids from about 177 to about 251 of SEQ ID NO:2; and
- (h) amino acids from about 180 to about 251 of SEQ ID NO:2.

47. (Withdrawn) The isolated nucleic acid molecule of claim 42, which is DNA.

48. (Withdrawn) A method of making a recombinant vector comprising inserting a nucleic acid molecule of claim 42 into a vector in operable linkage to a promoter.

49. (Withdrawn) A recombinant vector produced by the method of claim 48.

50. (Withdrawn) A method of making a recombinant host cell comprising introducing the recombinant vector of claim 49 into a host cell.

51. (Withdrawn) A recombinant host cell produced by the method of claim 50.

52. (Withdrawn) A recombinant method of producing a polypeptide, comprising culturing the recombinant host cell of claim 51 under conditions such that said polypeptide is expressed and recovering said polypeptide.

53. (Withdrawn) An isolated polypeptide comprising amino acids at least 95% identical to amino acids selected from the group consisting of:

- (a) amino acids from about 1 to about 251 of SEQ ID NO:2;
- (b) amino acids from about 2 to about 251 of SEQ ID NO:2;
- (c) amino acids from about 1 to about 24 of SEQ ID NO:2;
- (d) amino acids from about 25 to about 251 of SEQ ID NO:2;
- (e) amino acids from about 1 to about 175 of SEQ ID NO:2;
- (f) amino acids from about 1 to about 177 of SEQ ID NO:2;
- (g) amino acids from about 177 to about 251 of SEQ ID NO:2; and
- (h) amino acids from about 180 to about 251 of SEQ ID NO:2.

54. (Withdrawn) An isolated polypeptide wherein, except for at least one conservative amino acid substitution, said polypeptide has an amino acid sequence selected from the group consisting of:

- (a) amino acids from about 1 to about 251 of SEQ ID NO:2;
- (b) amino acids from about 2 to about 251 of SEQ ID NO:2;
- (c) amino acids from about 1 to about 24 of SEQ ID NO:2;
- (d) amino acids from about 25 to about 251 of SEQ ID NO:2;
- (e) amino acids from about 1 to about 175 of SEQ ID NO:2;
- (f) amino acids from about 1 to about 177 of SEQ ID NO:2;

- (g) amino acids from about 177 to about 251 of SEQ ID NO:2; and
- (h) amino acids from about 180 to about 251 of SEQ ID NO:2.

55. (Withdrawn) An isolated polypeptide comprising amino acids selected from the group consisting of:

- (a) amino acids from about 1 to about 251 of SEQ ID NO:2;
- (b) amino acids from about 2 to about 251 of SEQ ID NO:2;
- (c) amino acids from about 1 to about 24 of SEQ ID NO:2;
- (d) amino acids from about 25 to about 251 of SEQ ID NO:2;
- (e) amino acids from about 1 to about 175 of SEQ ID NO:2;
- (f) amino acids from about 1 to about 177 of SEQ ID NO:2;
- (g) amino acids from about 177 to about 251 of SEQ ID NO:2; and
- (h) amino acids from about 180 to about 251 of SEQ ID NO:2.

56. (Withdrawn) An epitope-bearing portion of the polypeptide of SEQ ID NO:2.

57. (Withdrawn) The epitope-bearing portion of claim 56, which comprises between 10 and 50 contiguous amino acids of SEQ ID NO:2.

58. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 53.

59. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 54.

60. (Withdrawn) An isolated antibody that binds specifically to the polypeptide of claim 55.

61. (Previously Added) The polypeptide of claim 12, wherein the arginine at position 179 is substituted by an amino acid that differs from arginine.

62. (Previously Added) The polypeptide of claim 61, wherein the amino acid at position 179 is glutamine.

63. (Previously Added) The polypeptide of claim 12, wherein the arginine at position 176 is substituted by an amino acid that differs from arginine.

64. (Previously Added) The polypeptide of claim 63, wherein the amino acid at position 176 is glutamine.

65. (Previously Added) The polypeptide of claim 12, wherein the amino acid at one or more of positions 175, 177, 178, and 180 is substituted by an amino acid that differs from the amino acid in the corresponding position of SEQ ID NO:4, wherein said polypeptide is not cleavable between amino acids 176 and 179 during expression.